

Evaluation of the effect of trypan blue on the corneal endothelium in cataract surgery

Trypan blue in cataract surgery

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Abstract

Aim: In this study, we aimed to evaluate the safety of 0.06% trypan blue applied to visualize the anterior capsule in cataract surgery.

Material and Methods: This single-center, prospective, randomized controlled study included 40 eyes of 20 patients. While performing cataract surgery on the right eyes of the patients, trypan blue was not used, and these eyes were evaluated as the control group. For the left eyes, trypan blue was used during surgery. The endothelial cell density (ECD) values of the two groups were measured, recorded, and analyzed at baseline and one week and one month after surgery, and their central corneal thicknesses were evaluated at baseline and one month after surgery.

Results: There was no statistically significant difference between the trypan blue and control groups in terms of the first-week ($p=0.852$) and first-month ($p=0.881$) ECD values and first-month pachymetry values ($p=0.218$). However, the ECD and pachymetry values significantly differed in both groups at one week and one month after surgery compared to the baseline ($p<0.001$).

Discussion: Our results showed that trypan blue injection into the anterior chamber to achieve comfortable and safe capsulorhexis in cataract surgery does not cause any adverse effects on the corneal endothelium.

Keywords

Cataract Surgery, Corneal Endothelial Cell Density, Trypan Blue

DOI: 10.4328/ACAM.21544 Received: 2022-12-10 Accepted: 2023-01-25 Published Online: 2023-01-26 Printed: 2023-02-01 Ann Clin Anal Med 2023;14(2):186-189

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This study was approved by the Ethics Committee of Health Sciences University Erzurum Regional Education and Research Hospital (Date: 2022-04-18, No: 2022/05-42)

Introduction

Cataract surgeons agree that the method of opening the anterior capsule should be capsulorhexis. Failure during capsulorhexis increases the risk of posterior capsule opening, vitreous loss, nucleus fall, and intraocular lens displacement during cataract surgery. It is very important to see the anterior capsule clearly in capsulorhexis, which is one of the basic parts of modern cataract surgery. However, the visualization of the anterior capsule is difficult during capsulorhexis in patients with white cataracts or in cases where the red reflex of the fundus cannot be obtained. Although many methods, including lateral illumination and radiofrequency capsulotomy have been developed to solve this problem, none of these techniques work very well.

Today, non-toxic dyes are used in cases where the anterior capsule cannot be selected well in the capsulorhexis stage. In 1993, McFarland and Hoffer were the first to report the injection of fluorescein under the capsule after the first capsulotomy. However, the use of fluorescein had certain disadvantages, such as the dye staining the surrounding tissues and passing into the vitreous. More recently, the dye injection technique has been modified with the use of indocyanine green and trypan blue. Trypan blue was first used by Melles in 1999. The lower cost, wider availability, and non-toxicity of trypan blue compared to other dyes have made it more popular [1].

In this study, we to evaluate whether 0.06% trypan blue applied to the anterior chamber of the eye to visualize the anterior capsule resulted in changes in the corneal endothelium after cataract surgery according to the evaluation under a specular microscope.

Material and Methods

This study had a prospective randomized controlled design. Forty eyes of 20 patients aged 40-80 years, who presented to the Ophthalmology Clinic of the Turkish Ministry of Health-Erzincan Binali Yıldırım University, were diagnosed with cataracts in both eyes requiring surgery, and had the same visual acuity were included in the study. Patients with the same degree of cataracts and equal vision reduction in both eyes were included in the sample. Preoperative cataract staging was evaluated with a slit lamp examination and graded using the four grading scales of the Lens Opacities Classification System III. The right eyes of the patients formed the control group, and the left eyes formed the study group. Ophthalmological examinations of all the patients were performed in detail before cataract surgery. In addition, corneal thickness and corneal endothelial measurements were performed using a specular microscope in all patients, and these values were recorded. Patients under the age of 40 and over the age of 80 years and those with any ocular pathology other than cataract were not included in the study. Cataract surgery was performed on both eyes of each patient by the same surgeon (K. B.) under the same microscope using the same phacoemulsification machine, first on the right eye and one week later on the left eye. During the operation, trypan blue was not used in the right eye, and 0.06% trypan blue was used in the left eye. All the operations were successfully completed with no complications. All the patients were followed up on the first day and in the first week and first month

postoperatively, and detailed ophthalmological examinations were performed. Corneal endothelial status was assessed using specular microscopy (CEM-530, Nidek, Gamagori, Japan), and endothelial cell density (ECD) (cells/mm²) was recorded. Corneal thicknesses were measured with an Al-Scan optical biometer (Nidek CO., Gamagori, Japan). During the follow-up, the corneal thickness and endothelial counts of each patient were measured and recorded. Ethical approval was obtained from the Clinical Research Ethics Committee of Health Sciences University Erzurum Regional Education and Research Hospital (18/04/2022, decision no: 2022/05-42). Written informed consent was obtained from all participants who participated in this study.

Statistical analysis

Statistical analyses were performed using SPSS v. 26. Categorical variables were expressed as numbers and percentages, and numerical variables as mean and standard deviation. The Mann-Whitney U test was used to compare the results between the two groups. The suitability of numerical variables for analysis was investigated with the Kolmogorov-Smirnov test. In the testing of the hypotheses, the Wilcoxon signed-rank test was used to compare numerical variables. The statistical significance level in all the analyses was accepted as $p < 0.05$.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

The mean age of the patients participating in the study was 69.05 ± 3.99 (min: 64, max: 79) years. Of the patients, 45.0% ($n = 9$) were female, and 55.0% ($n = 11$) were male. The visual acuity of the control group was 0.32 ± 0.12 (min: 0.1, max: 0.5), and that of the trypan blue group was 0.32 ± 0.12 (min: 0.1, max: 0.5) (Table 1).

A statistically significant difference was observed between the baseline ECD (cells/mm²) and the first-week and first-month ECD values within both groups ($p < 0.001$). There was also a statistically significant difference between the first-week and first-month ECD values ($p = 0.001$). Another statistically significant difference was observed in the corneal basal pachymetry (micron) values measured at one week after surgery and one month after surgery ($p < 0.001$).

There was no statistically significant difference between the control and trypan blue groups in terms of the first-

Table 1. Demographic features of the study participants.

| | Trypan blue group | Control group | P value |
|---------------------------------------|---------------------------|------------------|---------|
| Number of eyes | 20 | | - |
| Age (years) | 69.05 ± 3.99 (64-79) | | - |
| Male/female | 11/9 | | - |
| Best-corrected visual acuity (LogMAR) | 0.32 ± 0.12 (0.1-0.5) | | 0.65 |
| Intraocular pressure (mmHg) | 14.07 ± 2.94 | 14.66 ± 2.39 | 0.44 |
| Cataract grade | 2.1 ± 1.2 | 2.0 ± 1.2 | 0.85 |
| Operation time (min) | 15.6 ± 5.7 | 15.8 ± 4.4 | 0.64 |

Values are presented as mean \pm standard deviation (range). P-value: Mann-Whitney U test; inter-group comparison

Table 2. Postoperative corneal endothelial changes of the groups.

| | | Preoperative | First week | First month |
|---------------------------------|-------------------|-------------------|-----------------------------------|----------------------------------|
| ECD (cells/mm ²) | Trypan blue group | 2,426.30 ± 381.82 | 1,884.25 ± 607.85 (p < 0.001*) | 1845.50 ± 633.39 (p < 0.001†) |
| | Control group | 2,401.05 ± 373.92 | 1897.65 ± 495.19 (p < 0.001*) | 1941.75 ± 489.75 (p < 0.001†) |
| Pachymeter (micron) | Trypan blue group | 519.35 ± 18.81 | 554.80 ± 24.71 (p < 0.001*) | 537.0 ± 24.22 (p = 0.001†) |
| | Control group | 516.85 ± 15.39 | 541.45 ± 14.70 (p < 0.001*) | 525.35 ± 12.87 (p < 0.001†) |

* Wilcoxon signed-rank test; P-value for the comparison between the baseline and first-week measurements. † Wilcoxon signed-rank test; P-value for the comparison between the baseline and first-month measurements. ECD, endothelial cell density

week and first-month ECD values (p = 0.852). However, a statistically significant difference was observed in the first-week pachymetry values of the two groups (p = 0.018). The first-month pachymetry values did not statistically significantly differ between the two groups (p = 0.218) (Table 2).

Discussion

Trypan blue is currently used in many surgical operations in ophthalmology [2,3]. Capsule staining is important to achieve smooth anterior capsulorhexis in cataracts with a weak red reflex or no red reflex. Trypan blue is widely used due to its significant advantages over other dyes. It has long been used in cataract surgery, and its use has expanded to other anterior segment operations, such as trabeculectomy and corneal transplant. Although many surgeons have used trypan blue for many years, none of the large randomized clinical trials have specifically examined the effect of trypan blue on the corneal endothelium. Most reports on the safety of trypan blue belong to small case series or limited comparative studies without a control group.

In this study, cataract surgery was performed on both eyes of the same patients with the same level of cataracts in both eyes at an interval of one week. During cataract surgery, trypan blue was not used in the right eyes of the patients, while 0.06% trypan blue was used in the left eyes. In the study group, first air was applied to the anterior chamber, and then trypan blue was injected. In most studies in the literature, different patients were used to form study groups. However, in our study, we created our groups using the different eyes of the same patients to ensure that trypan blue was the only variable.

Similar to our design, Ucar et al. [4] used 1% trypan blue in one eye and did not use this dye in the contralateral eye while performing cataract surgery in patients with pseudoexfoliation. The authors found no significant difference between the preoperative and postoperative third-month ECD values. In addition, the central corneal thicknesses did not significantly differ between the two groups. Despite pseudoexfoliation, the corneal endothelium was not significantly affected by cataract surgery.

In a study evaluating patients with diabetic retinopathy and cataracts in both eyes, Abdelmotaal et al. [5] used trypan blue in one eye and did not use it in the other eye during cataract

surgery. They observed no significant difference in the ECD and corneal thickness values preoperatively and at the postoperative fourth week. Although endothelial loss was higher in diabetic patients, no additional toxic effect of trypan blue use was noted. In our study, we detected no significant difference between the trypan blue and control groups in terms of the first-week (1,884.25 ± 607.85 and 1,897.65 ± 495.19, respectively, p = 0.852) and first-month (1,845.50 ± 633.39 and 1,941.75 ± 489.75, respectively, p = 0.881) ECD values. Similarly, there was no significant difference in the central corneal thicknesses of the two groups in the first month after surgery. However, unlike Ucar et al [4], the first-week and first-month ECD values significantly differed compared to the baseline in both the trypan blue and control groups. This shows that cataract surgery performed with phacoemulsification reduces the number of cells in the corneal endothelium with or without the use of trypan blue, which is in agreement with other studies in the literature [6-10]. However, the use of trypan blue did not have an additional negative effect on the corneal endothelium. In the literature, different doses and application methods have been reported for the use of trypan blue in cataract surgery [7]. There is still no consensus regarding the ideal application form or dose. In our study, 0.06% dose and application under air were preferred.

There are certain limitations in this study. The study consisted of a small number of patients. Although all the operations were performed by the same surgeon and the same patients were used to form the study and control groups, the operation time and strength of phacoemulsification in different eyes of the same patients were not recorded.

Conclusion

In conclusion, the results of this study showed that the use of 0.06% trypan blue in cataract surgery was not toxic to the corneal endothelium. Further studies with a larger number of patients are needed to confirm our findings.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Funding: None

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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How to cite this article:

Bayrakceken Kemal, Utlü Bahadır. Evaluation of the effect of trypan blue on the corneal endothelium in cataract surgery. *Ann Clin Anal Med* 2023;14(2):186-189

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